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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/927,597	08/10/2001	Fady Malik	CYTOP018/1057	8190

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EXAMINER	
STEADMAN, DAVID J	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 03/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/927,597	MALIK ET AL.	
	Examiner	Art Unit	
	David J Steadman	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 January 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8-13* is/are pending in the application.

4a) Of the above claim(s) *11-13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8 and 9* is/are rejected.

7)☒ Claim(s) *10* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 August 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence Alignments*.

DETAILED ACTION

Status of the Application

[1] Claims 8-13 are pending in the application.

[2] Applicants' amendment to the claims, filed January 23, 2004, is acknowledged. This listing of the claims replaces all prior versions and listings of the claims.

[3] Claims 11-13 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

[4] Claims 8-10 are being examined on the merits.

[5] Applicants' arguments filed on January 23, 2004 have been fully considered and are deemed to be persuasive to overcome some of the rejections and/or objections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

[6] The text of those sections of Title 35, U.S. Code not included in the instant action can be found in a prior Office action.

Claim Objections

[7] In view of applicants' amendment to the claims, the objections to claims 8-10 as set forth in items [6] and [7] of the Office action mailed September 23, 2003 are withdrawn.

Claim Rejections - 35 USC § 112, First Paragraph

[8] The written description rejection of claims 8-9 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record as set forth in item [8] of the Office action mailed September 23, 2003 and for the reasons stated below. The examiner maintains the position that the single representative disclosed species, i.e., SEQ ID NO:2, fails to represent the entire genus of claimed human smooth muscle myosin heavy chain polypeptides (underline added for emphasis). It is noted that SEQ ID NO:6, 8, 10, 12, and 14 are subsequences of SEQ ID NO:2.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as be structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398 (Fed. Cir. 1997), quoting *Fiers v. Revel* , 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). Also, MPEP § 2163 states (citing *Amgen*, 927 F.2d at 1206, 18 USPQ2d at 1021), "A gene is a chemical compound, albeit a complex one, and it is well established in our law that conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials". In the instant case, the specification discloses a single human smooth muscle myosin heavy chain polypeptide described as SEQ ID NO:2 having ATPase and actin binding activity. This description also adequately describes a genus, within the sequence identity limitation of the instant claims (greater than 95% amino acid sequence identity to SEQ ID NO:2), of polypeptides having this particular function. Those sequences that are

"human" are a subset of this genus of polypeptides having greater than 95% amino acid sequence identity to SEQ ID NO:2 and having ATPase or actin binding activity. In this case, the specification fails to define those structural features of SEQ ID NO:2 that are commonly possessed by members of the genus that distinguish them from other "non-human" polypeptides. Thus, one skilled in the art cannot visualize or recognize the identity of the members of the genus. As such, this single representative species does not adequately describe this subset according to its structure so that one of skill in the art can visualize and distinguish those amino acid sequences that are human, particularly in view of the larger genus that includes both human and non-human sequences. Therefore, the instant claims are not adequately described.

Applicants argue that the specification satisfies the written description requirement by disclosing several relevant identifying characteristics, particularly structural and functional characteristics of the members of the genus. Applicants further argue that the instant claims are analogous to and are consistent with the conclusion reached in Example 14 of the Written Description Guidelines (hereafter referred to as "The Guidelines"). Specifically, applicants argue that claim 8 of the instant application is analogous to the claim of Example 14 as it links functional characteristics to structural characteristics. Applicants' argument is not found persuasive.

It should be noted that the genus of proteins as claimed in Example 14 of The Guidelines is not so limited to a subgenus of human polypeptides. Thus, contrary to applicants' argument, claim 8 is not analogous to the claim of Example 14 of The Guidelines. Claim 8 of the instant application is limited to a genus of human

polypeptides and the specification fails to convey the common structural characteristics of the single disclosed species of SEQ ID NO:2 such that one can visualize the members of the genus and distinguish a subgenus of "human" smooth muscle mysosin heavy chain polypeptides having greater than 95% identity and ATPase or actin binding activity from the broader genus of smooth muscle mysosin heavy chain polypeptides having greater than 95% identity and ATPase or actin binding activity. As such, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicant was in possession of the claimed invention.

[9] The scope of enablement rejection of claims 8-9 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record as set forth in item [9] of the Office action mailed September 23, 2003 and for the reasons stated below. The specification, while being enabling for the polypeptides of SEQ ID NO:2, 6, 8, 10, 12, and 14 does not reasonably provide enablement for the broad scope of claimed polypeptides, including all polypeptides having greater than 95% amino acid sequence identity to SEQ ID NO:2 and having ATPase activity or actin binding activity, and optionally wherein the polypeptide specifically binds to polyclonal antibodies generated against a polypeptide comprising SEQ ID NO:2, 6, 8, 10, 12, or 14.

Regarding the breadth of the claims, applicants argue that claim 8 has been amended to recite polypeptides with defined sequences and functions, i.e., SEQ ID NO:6, 8, 10, 12, and 14 or polypeptides having greater than 95% sequence identity to SEQ ID NO:2 and having ATPase activity or actin binding activity, and optionally

wherein the polypeptide specifically binds to polyclonal antibodies generated against a polypeptide comprising SEQ ID NO:2, 6, 8, 10, 12, or 14. Regarding the guidance provided in the specification, applicants argue that undue experimentation is not required to make and use the full scope of claimed polypeptides. Applicants argue that the experimentation required to make the full scope of claimed polypeptides is routine as methods for making the claimed polypeptide variants were known and methods of screening for variants having the recited activity were known. Applicants cite the reference of Creighton et al. ("Protein Structure: A Practical Approach", pages 184-185, IRL Press, New York, 1989) as allegedly providing support for their argument. Applicants' argument is not found persuasive.

The examiner maintains the position that undue experimentation is required to make the full scope of claimed polypeptides. As written, the claims broadly encompass all polypeptide variants having greater than 95% sequence identity to SEQ ID NO:2 and having ATPase activity or actin binding activity. Such variations include insertions, deletions, substitutions and combinations thereof to the sequence of SEQ ID NO:2 within the sequence identity limitation of the claim. There is no dispute that methods of altering a protein sequence and methods of screening for ATPase and actin binding activity were well known in the art at the time of the invention. However, neither the specification nor the prior art provides the necessary guidance for altering the amino acid sequence of SEQ ID NO:2 with an expectation of success for maintaining ATPase or actin binding activity. Such alteration(s) is/are HIGHLY unpredictable as evidenced by Branden et al. and Witkowski et al. (cited at page 7 of the Office action mailed

September 23, 2003), the teachings of which are undisputed by applicants. Even Creighton et al. (cited by applicants) acknowledge such unpredictability by disclosing, "without knowledge of the protein's tertiary structure, it is difficult to know which amino acid to change and which is the best residue to substitute for the desired functional and structural effect" (page 185, bottom to page 186, top). Furthermore, regarding claim 9, it is highly unpredictable as to whether an antibody that binds to a polypeptide *comprising* SEQ ID NO:2, 6, 8, 10, 12, or 14 will maintain the ability to bind an epitope within SEQ ID NO:2, 6, 8, 10, 12, or 14. Such unpredictability is evidenced by Abaza et al. (*J Prot Chem* 11:433-444) who teach that even alterations outside of a protein's antigenic site can negatively affect binding of an antibody to that antigenic site (page 433, right column to page 434, left column and page 438, right column). Thus, undue experimentation would be required to make the full scope of claimed polypeptides, particularly in view of the breadth of the claims, the lack of guidance and working examples in the specification, the high level of unpredictability in the art, and the amount of experimentation required.

Claim Rejections - 35 USC § 102

[10] Applicant's arguments traversing the instant rejections are addressed in item [14] below.

[11] The rejection of claims 8-9 under 35 U.S.C. 102(b) as being anticipated by Database GenPept Accession Number A41604 as set forth at item [12] of the Office action mailed September 23, 2003 is withdrawn in view of applicants' amendment to

claim 8 to limit the claimed polypeptide to an isolated human smooth muscle myosin heavy chain polypeptide (underline added for emphasis). Database GenPept Accession Number A41604 teaches a polypeptide that is isolated from rabbit and the examiner can find no teaching or suggestion in the prior art that would indicate the occurrence of an identical human orthologue of the protein of Database GenPept Accession Number A41604.

[12] The rejection of claims 8-9 under 35 U.S.C. 102(a) as being anticipated by Database GenPept Accession Number P35749 is maintained for the reasons of record as set forth in item [11] of the Office action mailed September 23, 2003 and for the reasons stated below. Claim 8 (in relevant part) is drawn to an isolated polypeptide having greater than 95% sequence identity to SEQ ID NO:2, wherein the polypeptide has ATPase or actin binding activity. Claim 9 limits the polypeptide of claim 8 to a polypeptide that specifically binds to polyclonal antibodies generated against a protein comprising SEQ ID NO:2, 6, 8, 10, 12, or 14. Database GenPept Accession Number P35749 teaches a polypeptide that is 98.9% identical to SEQ ID NO:2 with an actin-binding domain (see attached sequence alignment). This anticipates claims 8-9 as written.

[13] The rejection of claims 8-9 under 35 U.S.C. 102(b) as being anticipated by Database GenBank Accession Number AB020673 is maintained for the reasons of record as set forth in item [13] of the Office action mailed September 23, 2003 and for the reasons stated below. Claims 8 and 9 are drawn to an isolated polypeptide as described above. Database GenBank Accession Number AB020673 teaches a

polypeptide that is 98.9% identical to SEQ ID NO:2 (see attached sequence alignment). This anticipates claims 8-9 as written.

While Database GenBank Accession Number AB020673 does not specifically disclose their polypeptide as having ATPase activity or actin binding activity, such biological activities would be inherent properties of the polypeptide disclosed in Database GenBank Accession Number AB020673. Since the Office does not have the facilities for examining and comparing the claimed polypeptide with the polypeptide of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the polypeptide of the prior art does not possess the same material structural and functional characteristics of the claimed protein). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald* et al., 205 USPQ 594.

[14] Applicants argue the cited references do not disclose or suggest polypeptides that satisfy the limitations as recited in the claims. To the extent applicants' arguments apply to the reference of Database GenPept Accession Number A41604, the examiner agrees with applicants' argument (see item [11] above). However, regarding the references of Database GenPept Accession Number P35749 and Database GenBank Accession Number AB020673, applicants' argument is not found persuasive.

As evidenced in the attached sequence alignments, the cited references teach human polypeptides that have greater than 95% sequence identity to SEQ ID NO:2 and are expressly described as having ATPase or actin binding activity or inherently have ATPase or actin binding activity.

Conclusion

[15] Status of the claims:

- Claims 8-13 are pending.
- Claims 11-13 are withdrawn from consideration.
- Claims 8 and 9 are rejected.
- Claim 10 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.
- No claim is in condition for allowance.

Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (571) 272-0942. The Examiner can normally be reached Monday-Friday from 7:30 am to 4:00 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (571) 272-0928. The FAX number for submission of official papers to Group 1600 is (703) 308-4242. Draft or informal FAX communications should be directed to (571) 273-0942. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

David J. Steadman

Patent Examiner
Art Unit 1652
03-17-04